August 18, 2023

Dear Chairman Sanders, Ranking Member Cassidy, Chairman Rodgers, and Ranking Member Pallone:

On behalf of three major dietary supplement trade associations – the American Herbal Products Association (AHPA), the Consumer Healthcare Products Association (CHPA) and the United Natural Products Alliance (UNPA) – we wish both to thank you for your work to resolve the regulatory status of cannabidiol (CBD) products after enactment of the 2018 Farm Bill, and to provide comments on your Request for Information of July 27, 2023 (the July 27 RFI). Providing for the legal marketing and appropriate regulation of safe CBD products, including dietary supplement products, is of paramount importance to consumers, the medical community and responsible industry. Our comments, thus, are limited to a pathway for CBD dietary supplement products, and do not seek to address CBD in other product categories.

In sum, we have outlined below how existing Federal Food Drug and Cosmetic Act (FD&C Act) provisions and certain specific implementing regulations of relevant sections of the FD&C Act are adequate to regulate CBD dietary supplements. Application of these statutory provisions and regulations, however, would need to be predicated on the Secretary of Health and Human Services (the Secretary), or the Food and Drug Administration (FDA or the Agency) acting under the Secretary's authority, to waive the so-called "exclusionary clause" provisions[1] of existing law to allow marketing of CBD dietary supplements.[2]

As a matter of context, let us add some thoughts to the second paragraph of your letter. FDA's position on the regulation of CBD products has not been constant, and the Agency has only recently definitively stated its position that hemp-derived CBD may not be marketed as a food additive or dietary supplement. Indeed, the day the Farm Bill was enacted in 2018, then-Commissioner Gottlieb said, "Congress explicitly preserved the Agency's current authority to regulate products containing cannabis or cannabis-derived compounds under the Federal Food, Drug and Cosmetic Act (FD&CA Act) and section 351 of the Public Health Service Act. In doing so, Congress recognized the Agency's important public health role with respect to all the products it regulates. This allows FDA to continue enforcing the law to protect consumers and the public while also providing potential regulatory pathways for products containing cannabis and

[1] 21 U.S.C. § 321(ff)(3)(B)(i) and (ii).

[2] The July 27 RFI requests input on several questions related to the regulation of cannabidiol (CBD) in "foods, dietary supplements, tobacco, and cosmetics;" our response here is related only to regulating CBD in dietary supplement products."

cannabis-derived compounds." Notably, there was no reference to the Agency having inadequate authority to regulate CBD.

In April of 2019, Dr. Gottlieb announced a May public hearing as well as a high-level internal Agency working group that would study potential pathways for marketing of CBD containing products as dietary supplements and also as conventional foods. At that time, Dr. Gottlieb reiterated the language above about the Agency's current authority and the Agency titled his statement in terms of "potential regulatory changes." He said that the working group would consider options under current regulatory authorities and "consider whether there are legislative options that might lead to more efficient and appropriate pathways…." Dr. Gottlieb said that the group would begin sharing information with the public as early as summer 2019.[3]

In 2022 the Agency made public its view that additional legislative authority *might* be needed to regulate CBD. At a May 19, 2022 hearing before the House Appropriations Subcommittee on Agriculture, current Commissioner Dr. Califf said, "I don't think the current authorities [FDA has] on the food side or the drug side necessarily give us what we need to have to get the right pathway to move us forward."

Only on January 26 of this year did FDA definitively state it had concluded that the existing regulatory framework was not "appropriate" for CBD, stating it would work with Congress on a "new way forward."[4]

We have no compelling statistics to add to what you have received with respect to **Questions 1-3**, Current Market Dynamics, other than to point out that what had been a rise in CBD marketing has now abated, due to this uncertainty in regulatory status casting a long shadow over a once-promising marketplace fostered by the changes in the 2018 Farm Bill. Likewise, we have no data to add to **Questions 9-10, Federal-State Interaction** other than to add that differing state laws and regulations have also compounded the confusion in the marketplace, affecting both marketing and purchase of CBD products.

In addition, we wish to underscore that the exclusionary clause provisions you mention specifically allow the Secretary to issue a regulation, after notice and comment, finding that an article subject to these clauses, such as CBD, would be lawful. Clearly, the Congress did not intend the approval of an article as a new drug prior to its marketing as a dietary supplement to

[3] https://www.fda.gov/news-events/press-announcements/statement-fda-commissioner-scott-gottlieb-md-new-steps-advance-Agencys-continued-evaluation

[4] https://www.fda.gov/news-events/press-announcements/fda-concludes-existing-regulatory-frameworks-foods-and-supplements-are-not-appropriate-cannabidiol

automatically preclude its sale as a dietary supplement for all time. Resolution of the legal status of CBD through application of the Secretary's authority to grant an exception to the exclusionary clause provisions would solve one piece to the CBD regulatory puzzle, after which other challenges – including the key issue of product safety – can be addressed through existing laws and regulations.

To put things in perspective, as an overview, let us provide our views on the key points which we hope will guide your work as it progresses.

- Delay: The provision of the 2018 Farm bill that established a definition for "hemp," as differentiated from "marijuana," clarified that FDA retains the authority to regulate CBD products. In the almost five years since enactment of that law, the regulatory status of CBD products is no closer to being resolved than it was in 2018.

  Indeed, the Agency has progressed through a number of viewpoints since 2018 as we described above, first saying it was studying how to follow through on the Farm Bill descheduling of hemp products, then forming a working group, over three years later suggesting additional legislative authority may be needed, and finally in January of this year definitively seeking new legislative authority.

  Three major trade associations, the Consumer Healthcare Products Association (CHPA), the Council for Responsible Nutrition (CRN), and the Natural Products Association (NPA) submitted citizen petitions seeking to clarify CBD's regulatory status, outlining the basis for such regulation, and each was rejected years later by the Agency. The November 14, 2019 CHPA citizen petition was largely denied on January 26, 2023, with FDA agreeing only to continue to exercise its independent judgment to address emerging safety issues with CBD, "if any."[5] The June 16, 2020 CRN petition was similarly denied in its entirety on January 26, 2023; the NPA petition of February 21, 2022 was also denied on January 26, 2023.

  During this five-year time period, by any accounting, CBD products have proliferated in states and localities, becoming a significant mainstay of local commerce in many areas. There is no question that consumer demand exists for CBD products, which many seek in order to lead more healthy lifestyles. Yet beyond a few warning letters to companies making unallowed drug claims, FDA has taken little action to assure regulatory compliance or safety of these products.

[5] Response of Douglas W. Stearn, Deputy Center Director for Regulatory Affairs, Center for Food Safety and Applied Nutrition to David C. Spangler, Senior Vice President, Legal, Government Affairs & Policy and Anne Marie Murphy, Deputy General Counsel, Consumer Healthcare Products Association, January 26, 2023.

We can appreciate in some respects the reasons for FDA delay – the complexity of the issue, changes in Agency personnel, and limited resources being foremost contributors – but it is neither fair to consumers, manufacturers/marketers, farmers, or state regulators for these delays to continue.

We urge that you encourage FDA to "get to a yes" and establish the procedures by which CBD containing dietary supplements can be marketed under current law authority.

Following are the major areas we recommend for your attention as you consider your next steps.

- Harm reduction - Coincident to denial of the three citizen petitions, on January 26, 2023 Principal Deputy Commissioner Janet Woodcock, M.D. issued a statement, "FDA Concludes that Existing Regulatory Framework for Foods and Supplements are not Appropriate for Cannabidiol, Will Work with Congress on a New Way Forward."[6]

  More recently, we are aware that FDA has provided some in Congress with "technical assistance" on how a regulatory pathway for CBD could be drafted legislatively in the context of a new "harm reduction" program for all CBD products, not just dietary supplements. This "TA" is flawed in many respects, both in scope (covering all potential types of CBD products under one "harm reduction" scheme – an unwise idea for reasons we will detail later in this letter). We argue that Americans consume CBD in order to lead more healthy lives – it is that approach that should guide the regulation of these products, rather than a "harm reduction" approach similar to the known carcinogen tobacco. In addition, such a pathway would take a very long time to fully implement, when, as discussed in more detail below, appropriate and effective regulation of dietary supplements containing CBD can and should be put in place much more rapidly at less expense through application of the current regulatory framework.

- There is ample authority under the FD&C Act for effective regulations of dietary supplement products containing CBD. The basic federal statutory framework rests on a safety paradigm, with additional requirements for labeling, content, and serious adverse event reporting. We respond to your **Question 4 in** much greater detail below.

- Attempting to regulate all CBD products under one scheme would engender unnecessary delay and cost. As we make clear in this letter, substantial authority for CBD dietary supplements already exists. That authority could be amplified upon or adjusted, if necessary (for example, to address intoxicants or set requirements for limited duration use labeling),

[6] https://www.fda.gov/news-events/press-announcements/fda-concludes-existing-regulatory-frameworks-foods-and-supplements-are-not-appropriate-cannabidiol

but existing authority is largely applicable to CBD products. Similarly, Congress just last year enacted a new regulatory paradigm for cosmetics, which could serve as a basis for CBD containing cosmetic products. There is no more need to "reinvent the wheel" to create a CBD paradigm across product categories than there is, for example, in regulating caffeine.

- Better FDA enforcement must be paramount. Many of the citizen petitions urged such enforcement; the Agency did not comment, saying that enforcement was not within the ambit of citizen petitions. Nonetheless, this does not make the issue go away.

- Safety: As we will detail later in our comments, the structure of the FD&C Act, as amended by the Dietary Supplement Health and Education Act in 1994, allows abundant consumer safeguards to protect against consumption of unsafe products. Where the Agency finds those lacking, we welcome a dialog with you and FDA officials.

  Further, in the years since enactment of the 2018 Farm Bill, millions of Americans may have been exposed to unsafe products. Surely this should be a major focus of FDA. We are not aware that any budget request has been made for better enforcement resources.

- Regulation in other countries: Although it was not addressed in your letter, we commend to your attention a consideration of how other countries are dealing with sales of CBD. Regulators in a number of countries outside of the U.S. have achieved progress toward a successful balance between consumer access and safety while using existing regulatory frameworks. Notably, the EU and UK have implemented strategies that ensure thorough safety assessments for CBD products while permitting their marketing.

  For example, CBD extract products are categorized as novel foods in the EU and UK, adhering to stringent manufacturing and safety standards not unlike those relevant to new dietary ingredients (NDIs) in the U.S. In Northern Ireland, CBD extracts require explicit EU law authorization prior to market entry. To secure this authorization, businesses must submit detailed safety applications for CBD extracts, isolates, and related products. This process mirrors the NDI approach, fostering consistent production methods and safety evidence for each authorized ingredient.

  To maintain market stability, the Food Standards Agency allowed CBD products linked to novel food applications that met specific criteria to continue being sold. The provision's cutoff date was announced on February 13, 2020, with a requirement to submit authorization applications by March 31, 2021. Products with valid or progressing applications could remain available.

This regulatory framework ensures that all CBD products adhere to legislative requirements, encompassing accurate labeling, safety, and avoiding classification as controlled substances. Products not meeting these standards or absent from the authorized list were to be withdrawn from the market.

The UK's Food Standards Agency additionally provided practical consumer advice grounded in scientific evidence, urging cautious CBD use—particularly for vulnerable groups—and noting potential liver impact from higher doses. To this end, a recommended daily limit of 70 mg for healthy adults was advised, with acknowledgment that available evidence points to potential health risks beyond this threshold.

The comprehensive approach of the EU and UK reflects a commitment to ensuring consumer safety without impeding CBD product access. This model offers valuable lessons for FDA to consider in crafting a more effective regulatory framework for CBD in the United States.

Similarly, Health Canada acknowledges the necessity of responsible CBD product regulation, striving to balance consumer access and safety. Health Canada's external Science Advisory Committee on Health Products Containing Cannabis draws insights from the UK and EU models, shaping recommendations that prioritize safe usage for healthy adults.

These guidelines recommend CBD doses from 20 mg/day to a maximum of 200 mg/day for short-term use by healthy adults, emphasizing pharmacist consultation for potential CBD interactions. Products should clearly detail interactions and be avoided during pregnancy and lactation. Prominent labels must caution against CBD use during pregnancy due to potential fetal development effects.

Moreover, Health Canada's recommendations align with UK and EU frameworks, ensuring consumer safety while promoting public education. These campaigns clarify benefits, risks, safety information, and research gaps, ensuring equitable access for all Canadians.

In late 2020, the Therapeutic Goods Administration (TGA) made a significant change in Australia, reclassifying certain low-dose CBD preparations from Prescription Medicine to Pharmacist Only Medicine. TGA-approved low-dose CBD products, up to 150 mg/day, can now be supplied over the counter by pharmacists. Specific requirements for dosage form, packaging, and child-resistant closures accompany this reclassification.

Unlike FDA, which has faced criticism for its CBD regulation, global regulators showcase successful models that balance consumer access and safety. The EU, UK, Canadian, and Australian approaches offer insights for effective CBD regulation, maintaining safe

accessibility while ensuring informed consumer choices. These examples illuminate a path for FDA to enhance its regulatory framework for CBD products in the United States , under its current authority and without the need for the Congress to create a new regulatory pathway.

We next turn to several of your specific questions in the July 27 RFI, confined to regulating CBD in dietary supplement products.

Response to Question 4- Pathway:
As noted previously, while the July 27 RFI requests input on several questions related to the regulation of cannabidiol (CBD) in "foods, dietary supplements, tobacco, and cosmetics," our response here is related only to regulating CBD in dietary supplement products.[7]

Many of the questions, particularly **Questions 4 and 5**, relate to the existing, robust framework under which all dietary supplements are regulated by FDA. That same framework can be readily applied to dietary supplements that consist of or contain hemp or CBD ingredients identified in the definition of a "dietary supplement" at Section 201(ff)(1) of the Food, Drug, and Cosmetic Act (21 U.S.C. § 321(ff)(1)[8]). This existing dietary supplement framework, if applied to CBD dietary supplements, would ensure such products are lawfully produced and reasonably expected to be safe for their intended uses.

Statutory restrictions apply to marketing of any article that meets the definition of a "dietary supplement" under federal law but that, in relevant part, has been approved as a new drug[9] or authorized for investigation as a new drug,[10] if such article was not previously marketed as a dietary supplement or as a food (hereinafter the exclusionary clause provisions). Both such provisions provide FDA, acting under the authority of the Secretary of Health and Human Services (the Secretary), the authority to issue a regulation, after notice and comment, that would grant an exception to either exclusionary clause provision. Neither the Secretary nor FDA acting under the Secretary's authority have to date acted to implement this authority to grant such an exception for CBD. The comments provided here describe the existing regulatory tools that FDA already has at its disposal if the Secretary or the Agency acting under the Secretary's authority does, in fact, grant exceptions to the exclusionary clause provisions for CBD.

[7] Although we are not providing any comments on regulating CBD in conventional foods, tobacco products, or cosmetics, it may be that the existing regulatory frameworks these classes are also more than adequate, such that there may be no need or new regulatory pathways for such goods.

[8] Hereinafter these comments will reference only relevant sections and paragraphs of the U.S. Code.

[9] 21 U.S.C. § 321(ff)(3)(B)(i).

[10] 21 U.S.C. § 321(ff)(3)(B)(ii).

Inclusion in the definition of "dietary supplement."

Continuing on **Questions 4 and 5**, the hemp plant itself (and its physical parts, primarily the flowering tops and seeds) is an "herb or other botanical," per 21 U.S.C. § 321(ff)(1)(C); constituents of the hemp plant, such as CBD, are included in the "dietary supplement" definition at § 321(ff)(1)(F)[11]; and extracts of the hemp plant, such as tinctures and other ingredients obtained through extraction of hemp with solvents such as water, ethanol, and CO_2, are also included in the "dietary supplement" definition at § 321(ff)(1)(F).

Thus, current statutory definitions already apply to hemp and its extracts and naturally occurring constituents, including CBD, such that there is no need for a new regulatory pathway to include these ingredients in dietary supplements.

Requirement for food facility registration.

All domestic and foreign facilities that manufacture, process, pack, or hold food for human or animal consumption in the United States are required to register these facilities with FDA, and to update these registrations every two years.[12]

FDA established a final rule to implement this statutory requirement on October 3, 2005.[13] The rule clarifies that the facility registration requirement applies to the dietary supplement class of foods and to the dietary ingredients included in dietary supplements.[14]

FDA has also issued guidance on food facility registrations, including final guidance on food product categories required to be identified in these registration[15] (hereinafter the 2016 Food Product Categories Guidance). Changes made to the facility registration requirements in the 2016

[11] The "constituents" referred to in this response are limited just to those that are naturally occurring in the hemp plant and extracted directly from hemp plant biomass, and do not extend to any constituent produced synthetically or semi-synthetically. FDA itself has taken the position that synthetic constituents are not dietary ingredients: "Under a plain reading of the FD&C Act, a synthetic copy of an herb or other botanical does not qualify as a dietary ingredient under section 201(ff)(1)(C) of the FD&C Act. … A substance that has been synthesized in a laboratory or factory has never been part of an herb or other botanical and, therefore, is not a dietary ingredient under section 201(ff)(1)(C) of the FD&C Act." *Dietary Supplements: New Dietary Ingredient Notifications and Related Issues: Guidance for Industry*. Draft Guidance, August 2016 at page 38. Thus, the current regulatory framework has already addressed the subject of synthetic constituents, such that a new regulatory pathway is not needed for this purpose.

[12] 21 U.S.C. § 350d.

[13] 21 C.F.R. Part 1, Subpart H – Registration of Food Facilities (21 C.F.R. § 1.225 et seq.). Published as an interim final rule on October 10, 2003 (68 Fed. Reg. 58,894) and confirmed as a final rule on October 3, 2005 (70 Fed. Reg. 57,505).

[14] Paragraph (2) of the definition of "food" in 21 C.F.R. § 1.227 states in relevant part: "Examples of food include: … dietary supplements and dietary ingredients…."

[15] Necessity of the Use of Food Product Categories in Food Facility Registrations and Updates to Food Product Categories (2016 Edition): Guidance for Industry. September 2016.

Food Product Categories Guidance are directly relevant to this response to the July 27 RFI. Specifically, FDA revised this guidance to move certain subcategories of dietary supplements from optional disclosure to mandatory disclosure, including "Herbals and Botanicals." Importantly, FDA also included the following statement in the 2016 Food Product Categories Guidance:

> "To comply with the GGP regulations [FDA's good guidance practice regulations] and make sure that regulated entities and the public understand that guidance documents are nonbinding, FDA guidances ordinarily contain standard language explaining that guidances should be viewed only as recommendations unless specific regulatory or statutory requirements are cited … FDA is not including this standard language in this guidance because it is not an accurate description of the effect of this guidance. This guidance contains findings that serve as the predicates for binding requirements on industry."

Thus, current statutory controls, final regulations, and FDA guidance already require registration of all facilities that manufacture, process, pack, or hold food for human or animal consumption in the United States, including foods that are dietary supplements. In addition, FDA has indicated by its issuance of the 2016 Food Product Categories Guidance that it has sufficient authority to amend the food facility regulations to require disclosure in registrations of specific categories of foods, including specific subcategories of dietary supplements. FDA could, simultaneous to issuance by the Secretary or by FDA acting under the Secretary's authority of a regulation to grant exceptions for CBD to the exclusionary clause provisions and operating on the Agency's existing authority, again amend its guidance on food facility registrations to require dietary supplement operations to disclose any CBD products as a subset of the currently mandated "Herbals and Botanicals" subset of dietary supplements.

There is therefore no need for a new legislatively created regulatory pathway to ensure that FDA is provided with all information deemed necessary for facilities that manufacture, process, pack, or hold CBD containing dietary supplements.

*As to **Questions 20 and 21** concerning quality, the dietary supplement cGMP rule ensures product quality and protects against contaminants.* FDA established its final rule on Current Good Manufacturing Practice in Manufacturing, Packaging, Labeling, or Holding Operations for Dietary Supplements (the dietary supplement cGMP rule) in June 2007, codified at 21 C.F.R. Part 111.[16] Full compliance with this regulation has been mandatory since June 2010 for all such dietary supplement operations, including small business operations. Under the existing regulatory framework, this rule would therefore apply to all manufacturing, packaging, labeling, and holding operations for dietary supplements that consist of or contain hemp or CBD.

[16] 72 Fed. Reg. 34,752 (June 25, 2007).

At the heart of the dietary supplement cGMP rule are requirements to establish a number of specifications for each finished dietary supplement, including specifications for identity, purity, strength, and composition, and for limits on those types of contamination that may adulterate or lead to adulteration of the finished product.[17] Dietary supplement operations are also required to confirm that all established finished product specifications are met.[18]

One contaminant that may adulterate a hemp or CBD dietary supplement is the naturally occurring delta-9 tetrahydrocannabinol (delta-9 THC) present in the hemp plant; by the definition established in the 2018 Farm Bill, the level of delta-9 THC in hemp may not exceed 0.3% on a dry weight basis.[19] A manufacturer of a dietary supplement that consists of or contains a hemp or CBD ingredient could establish its own specification for the level of delta-9 THC in its finished product, for example as "not detected" or at a quantitative level established under regulations promulgated by one or more state regulators. Alternately, FDA could dictate such a limit in notice and comment rulemaking at such time as the Secretary or FDA acting under the Secretary's authority initiates action to grant an exception to the exclusionary clause provisions. By establishing and confirming a quantitative specification for delta-9 THC, or for total THC (including tetrahydrocannabinol acid (THCA)) if more appropriate, compliance with this detail in the existing dietary supplement cGMP rule will ensure that each hemp and CBD dietary supplement contains only a very low level of delta-9 THC, or total THC.

Thus, FDA's current regulatory framework, and specifically the dietary supplement cGMP rule at 21 C.F.R. Part 111, if applied to hemp and CBD dietary supplements, will ensure the quality of such finished products and protect against excessive levels of THC or total THC. There is therefore no need for a new regulatory pathway to control manufacturing of hemp and CBD dietary supplements.

Existing requirements to submit reports of serious adverse events associated with dietary supplements protect consumer safety, which speaks to a number of safety-related ***Questions****.*
The Dietary Supplement and Nonprescription Drug Consumer Protection Act was enacted in 2006 and has required submission to FDA of any and all reports received by marketers of dietary supplements of serious adverse events associated with their products. The signatories to this

[17] 21 C.F.R. § 111.70(e). Specifications are also required to be established for certain points, steps, and stages in the manufacturing process; for the identity and other specifications for all dietary ingredients and other components; for the in-process production; for labels and packaging; and for several other criteria as may be necessary for specific operations. Additional details can be provided upon request.

[18] 21 C.F.R. § 111.75(c) and (d). The dietary supplement cGMP rule also requires operations to confirm that all other established specification are met.

[19] 7 U.S.C. § 1639o(1).

response to the July 27 RFI all supported this legislation when it was introduced in the 109th Congress.

For purposes of this 2006 law, a serious adverse event (SAE) is defined, in language that is quite similar to the definition of a serious adverse event for drug products,[20] as a health-related event associated with the use of a dietary supplement that results death; a life-threatening experience; inpatient hospitalization; a persistent or significant disability or incapacity; or a congenital anomaly or birth defect; or one that requires, based on reasonable medical judgment, a medical or surgical intervention to prevent any of the outcomes described above.[21] In order to comply with this requirement, marketers of dietary supplements must have systems in place to internally track ***all*** adverse events, whether serious or otherwise. These records are available to FDA in routine inspections, and this would immediately be the case for CBD dietary supplements were FDA to grant an exception to the exclusionary clause provisions for CBD.

FDA could today, in rulemaking by the Secretary or FDA acting under the Secretary's authority, exercise its authority to grant an exception to the exclusionary clause provisions, establish an affirmative responsibility for all marketers of dietary supplements consisting of or containing CBD to submit any reports received of serious adverse events associated with such products. There is therefore no need for a new regulatory pathway to ensure that this important protection applies to CBD containing dietary supplements.

*On **Question 25**, label warnings are specifically allowed for dietary supplements.*
The Dietary Supplement Health and Education Act (DSHEA) amended the Food, Drug, and Cosmetic Act in several ways upon its enactment in 1994. One of DSHEA's many important amendments was to establish that "A dietary supplement shall not be deemed misbranded solely because its label or labeling contains directions or conditions of use or warnings."[22] The Congress included this language to counter the fact that "FDA had occasionally taken the position in the past that such label information rendered the supplement a drug," and noted that, "Consumers are afforded greater protection when more information is provided."[23]

There are today examples of FDA requiring warning statements on certain dietary supplements. For example, any dietary supplement in solid oral dosage form (e.g., tablets or capsules) that contains iron or iron salts for use as an iron source must place a specific warning statement on the product label, as follows:

[20] 21 C.F.R. § 314.80(a).

[21] 21 U.S.C. § 379aa-1.

[22] 21 U.S.C. § 343(s).

[23] Senate Report 103-410 (to accompany S. 784), October 8, 1994.

> "WARNING: Accidental overdose of iron-containing products is a leading cause of fatal poisoning in children under 6. Keep this product out of reach of children. In case of accidental overdose, call a doctor or poison control center immediately."[24]

Similarly, when FDA announced its decision to authorize the use of health claims on the association between soluble fiber from psyllium seed husk and reduced risk of coronary heart disease (CHD)[25], the Agency simultaneously established a labeling regulation for foods containing dry or incompletely hydrated psyllium husk and bearing the authorized claim of reduced CHD, to require a label statement informing consumers of risks associated with consuming such products without adequate water. The regulation provides the following language as an example of the required label statement:

> "NOTICE: This food should be eaten with at least a full glass of liquid. Eating this product without enough liquid may cause choking. Do not eat this product if you have difficulty in swallowing."

The signatories to these comments to the July 27 RFI conducted an informal review of representative psyllium dietary supplements bearing this authorized health claim and marketed on Internet websites in early August 2023[26] and found that each reviewed product does include the required statement, generally with the word "food" substituted with the word "products," on product labels and websites where these products are sold.

More recently, FDA issued a public notice in June 2019 "warning consumers about safety concerns regarding an ingredient called vinpocetine that is found in dietary supplements, specifically concerns about the use of this ingredient by women of childbearing age."[27] With this notice, FDA advised pregnant women and women who could become pregnant not to take vinpocetine, and also stated it was "advising firms marketing dietary supplements containing vinpocetine to evaluate their product labeling to ensure that it provides safety warnings against use by pregnant women and women who could become pregnant." The signatories to these comments to the July 27 RFI conducted an informal review of representative vinpocetine dietary

[24] 21 C.F.R. § 101.17(e)(1).

[25] 63 Fed. Reg. 8,103 (February 18, 1998).

[26] The signatories hereto do not represent this informal review to be a complete review of all dietary supplements that bear this authorized health claim.

[27] Abernathy, A. (Principal Deputy Commissioner - Office of the Commissioner). FDA Statement: Statement on warning for women of childbearing age about possible safety risks of dietary supplements containing vinpocetine. June 3, 2019.

supplements marketed on Internet websites in early August 2023[28] and found that all reviewed products do include the suggested safety warnings on product labels and websites where these products are sold.[29]

More generally, in promulgating the final rule on dietary supplement structure-functions claims,[30] FDA observed that the labeling of dietary supplements must present any information that is "material" to ensure safe use of these products, and restated this statutory obligation in several locations in the preamble to that final rule, as follows:

> "The Agency also notes that there may be important health-related consequences associated with taking a dietary supplement, even if the product does not bear disease claims. For the labeling of a dietary supplement to be considered truthful and non-misleading (see sections 403(a) and (r)(6) and 201(g)(1) of the act), it must include all information that is material in light of the claims made for the product and the consequences that may result from its use (see section 201(m)) of the act."[31]

> "Although the act does not prescribe any specific statements concerning adverse reactions or contraindications that dietary supplements must carry, the Agency notes that dietary supplement labeling, like the labeling of all other FDA-regulated products, is required to include all information that is material in light of consequences that may result from the use of the product or representations made about it (see sections 403(a)(1) and 201(n) of the act)."[32]

> "FDA agrees that it is important to inform consumers about potential adverse effects or drug interactions for specific dietary supplement ingredients. In fact, dietary supplement labeling, like the labeling of other FDA-regulated products, is required to include all facts that are material in light of consequences that may result from use of the product or representations made about it (sections 403(a)(1) and 201(n) of the act). This provision is not intended in any

[28] The signatories hereto do not represent this informal review to be a complete review of all vinpocetine dietary supplements.

[29] Label statements identified include, for example: "Do not use if you are of childbearing age, pregnant or planning to become pregnant" and "Do not take this product if you are pregnant, may become pregnant, or are nursing."

[30] Regulations on Statements Made for Dietary Supplements Concerning the Effect of the Product on the Structure or Function of the Body. 65 Fed. Reg. 1,000 (January 6, 2000).

[31] 65 Fed. Reg. 1,000 (January 6, 2000) at 1,005.

[32] 65 Fed. Reg. 1,000 (January 6, 2000) at 1,007.

> way to preclude truthful adverse event or drug interaction information from appearing in a dietary supplement's labeling."[33]

In this same rulemaking, FDA also acknowledged that inclusion of a specific structure-function claim in an over the counter (OTC) drug monograph does not preclude use of the same structure-function claim for a dietary supplement product, and then reiterated the statutory obligation to provide labeling for any such product that presents all information that is "material" to ensure safe use of these products, as follows:

> "… in light of the statutory requirement that dietary supplements bear all information that is material in light of consequences that may result from use of the product or representations made about it, dietary supplements that contain or are labeled as containing ingredients covered by an OTC monograph and that are being sold for the claims covered by the monograph may be misbranded to the extent that they omit material information required under the monograph. For example, if the OTC monograph required a label statement that products containing a particular ingredient should not be used by persons taking a prescription monoamine oxidase inhibitor, a dietary supplement containing that ingredient would be misbranded if its label did not include such statement."[34]

It is obvious from this review of the use of label warnings on marketed dietary supplements that such label warnings are lawful; that FDA understands that such statements are both lawful and required when necessary to provide information that is material to safe use of a dietary supplement; and that FDA also understands its current authority extends to recommending warning on dietary supplements, and in fact has used that authority under the current regulatory framework for dietary supplements.

In the case of CBD, FDA has identified concerns about its use by certain populations, including children and pregnant women. Under its current regulatory authority, FDA could recommend or require label warnings to direct against use by, for example, children, pregnant women, or other specific populations, and to provide other material information that is developed through a science-based process. There is therefore no need for a new regulatory pathway to make sure that dietary supplements that consist of or contain CBD as a dietary ingredient provide any needed warning.

Further to **Question 25**, as further protection for young children, as with any dietary supplement, the Consumer Product Safety Commission (CPSC) could require child-resistant packaging for CBD

[33] 65 Fed. Reg. 1,000 (January 6, 2000) at 1,023.

[34] 65 Fed. Reg. 1,000 (January 6, 2000) at 1,031.

containing products to protect children from serious illness or injury.[35] Dietary supplements containing iron, for instance, are required to use child-resistant packaging.[36] CPSC consulted with FDA when both took action on labeling and packaging for dietary supplements with iron in the late 1990s.

The statutory provisions for new dietary ingredients protect public health, further addressing the ***Questions*** *specific to safety.*

Any dietary ingredient that was not marketed in the United States before October 15, 1994 is defined by stature as a "new dietary ingredient" (NDI).[37] Dietary supplements that contain an NDI are adulterated under current law if there "is inadequate information to provide reasonable assurance that such ingredient does not present a significant or unreasonable risk of illness or injury,"[38] or "unless it meets one of the following requirements:

> "(1) The dietary supplement contains only dietary ingredients which have been present in the food supply as an article used for food in a form in which the food has not been chemically altered.
>
> "(2) There is a history of use or other evidence of safety establishing that the dietary ingredient when used under the conditions recommended or suggested in the labeling of the dietary supplement will reasonably be expected to be safe and, at least 75 days before being introduced or delivered for introduction into interstate commerce, the manufacturer or distributor of the dietary ingredient or dietary supplement provides the Secretary with information, including any citation to published articles, which is the basis on which the manufacturer or distributor has concluded that a dietary supplement containing such dietary ingredient will reasonably be expected to be safe."[39]

FDA promulgated regulations to create a framework for submission of the information identified in paragraph (2) above in a final rule published in September 1997 and codified at 21 C.F.R. § 190.6.[40]

[35] See Poison Prevention Packaging Act at 15 U.S.C. Section 1471, et seq.16 CFR 1700.14(a)(13).

[36] 16 CFR 1700.14(a)(13).

[37] 21 U.S.C. § 350b(d).

[38] 21 U.S.C. § 342(f)(1)(B).

[39] 21 U.S.C. § 350b(a).

[40] 62 Fed. Reg. 49,886 (September 23, 1997).

FDA has not to date declared CBD to be an NDI. It has, however, implied this status for CBD, in discussing the exclusionary clause provisions of the FD&C Act by stating that CBD was not, "based on available evidence," marketed as a dietary supplement prior to the date that new drug investigations were authorized for CBD.[41] Since the date of these authorizations occurred after October 15, 1994, the obvious implication is that FDA believes that "based on available evidence" CBD is an NDI.

These comments neither agree nor disagree with FDA's assertion as to whether CBD was marketed prior to the earliest date of a new drug investigation authorization, and do not take a position as to whether or not CBD is an NDI. Nonetheless, a manufacturer or distributor of a CBD ingredient that is in fact an NDI is currently required to ensure that dietary supplements that contain such an NDI are not adulterated through one of the existing statutory provisions.

Thus, the current regulatory framework for any CBD ingredient that is a new dietary ingredient already dictates the legal obligations for bringing such an ingredient to the market. There is therefore no need for a new regulatory pathway to accomplish this purpose.

Conclusions

The signatories hereto recognize that the article CBD may not currently be used as an ingredient in dietary supplements due to the "exclusionary clause provisions" of the FD&C Act, but also assert that the Secretary, or FDA acting under the Secretary's authority, could today, under the existing regulatory framework, initiate notice and comment rulemaking to grant an exception to the exclusionary clause provisions for use of CBD in dietary supplements.

We also assert that there is nothing to prevent FDA from granting this exception with whatever conditions it may establish, through a science-based process, as necessary to ensure that CBD containing dietary supplements are reasonably expected to be safe. The Agency could, for example, grant this exception only for dietary supplements that contain no more than a specified quantitative limit of CBD and of delta-9 THC (or total THC), and that contain only plant-derived cannabinoids. The Agency could also limit an exception to the exclusionary clause provisions to CBD dietary supplements that are labeled with appropriate warning or usage instructions, for example, to exclude certain populations, such as children and pregnant women, or to limit dosage and duration of use.

As articulated in detail above, FDA could today, under its current authority and in the existing regulatory framework, move CBD containing dietary supplements out of the shadows and into the bright light of regulatory compliance. We therefore strongly discourage your committees from

[41] See for example, Question #10 in the Questions and Answers section of the FDA webpage titled, FDA Regulation of Cannabis and Cannabis-Derived Products, Including Cannabidiol (CBD), content current as of 07/05/2023.

creating a "new regulatory pathway" for CBD containing dietary supplements, in spite of FDA's request that you take such action. If any legislative action is needed to protect the millions of Americans who are already consuming CBD dietary supplements, it should be legislation that directs FDA to promptly initiate rulemaking to grant an exception to the exclusionary clause provisions for CBD as a dietary supplement, with appropriate controls, under the existing regulatory framework.

We greatly appreciate the opportunity to provide comments on the important matter of appropriate federal regulatory controls for consumer products that contain CBD, and we can be available to meet with you to discuss this further if that would be useful.

Sincerely,

Michael McGuffin
President, American Herbal Products Association

Scott Melville
President & CEO, Consumer Healthcare Products Association

Loren Israelsen
President, United Natural Products Alliance